UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte JOSEPH D. MOSCA

Appeal No. 2005-0402
Application No. 09/638,358

ON BRIEF

ELLIS, SCHEINER and GREEN, Administrative Patent Judges.

ELLIS, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal pursuant to 35 U.S.C. § 134 from the examiner's final rejection of 19-39, all the claims pending in the application. Claims 1-18 have been canceled.

As a preliminary matter, we note that the claims on appeal were subject to an election of species requirement in the Office action mailed on December 19, 2001. In response, the appellant elected to prosecute the species "MHCII" (Major Histocompatibility Complex class II) for examination. See, the appellant's Transmittal Letter, received January 24, 2002.

Accordingly, for purposes of this appeal, we have considered the issues as they apply to the "MHCII" complex. Claims 19 and 29 are representative of the subject matter on appeal and read as follows:

> 19. A composition comprising a mesenchymal stem cell that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a member selected from the group consisting of MHCII, MHCI, and CDI such that said at least one antigen is presented to initiate an immune response.
>
> 29. A composition comprising a cell of the adipocyte lineage that expresses at least one co-stimulatory molecule, and has been modified to have at least one exogenous antigen fragment bound to a primary surface molecule of said cell such that said at least one antigen is presented to initiate an immune response.

The examiner relies on the following references:

Gerson et al. (Gerson)	5,591,625	Jan. 7, 1997
Robinson	5,962,320	Oct. 5, 1999

Claims 19-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Robinson in view of Gerson.

We have carefully considered the respective positions of both the appellant and the examiner and find ourselves in substantial agreement with that of the appellant. Accordingly, we reverse.

Background

The present invention is directed to stem cells which have been genetically-engineered to induce an immune response to at least one antigen. It is well known in the art that antigens are processed by certain antigen-presenting cells. See, the specification, p. 1. To that end, the specification discloses that:

> In order to trigger an efficient immune response, antigens must first be processed by an antigen-presenting cell (APC) that degrades the antigen and "presents" the resulting antigen fragments to other cells involved in the immune response. Macrophages are among the most commonly encountered type of APC; other examples include dendritic cells in the spleen and Kupffer cells in the liver. Macrophages readily engulf foreign particles and cells by the process of phagocytosis. Although all macrophages are avid phagocytes, only some can process foreign antigens in a way that stimulates an immune response. The macrophages that perform this function carry specialized plasma membrane glycoproteins called major histocompatibility complex (MHC) molecules. In man the MHC is known as HLA. MHC molecules reside only on the surfaces of cells involved in immune responses [Specification, p. 1].

During the processing of an antigen by a macrophage, the antigen is degraded into peptide fragments 10-20 amino acids in length. Specification, p. 2, para. 1. These peptide fragments become "bound to MHC class II molecules, which possess an antigen-binding cleft that is specifically designed to hold antigen fragments." Id. The "foreign antigen-MHC II complex is then transported to the cell surface for 'presentation' to other cells of the immune system." Id.

To stimulate a T cell response, however, the foreign antigen-MHC II complex must be co-delivered with a co-stimulatory signal by a specialized antigen-presenting cell. Specification, p. 2, last para. Glycoproteins B7-1 and B7-2 are said to be

examples of co-stimulatory molecules. Id., p. 3, para. 2. According to the specification, B7-1 and B7-2 are

> homodimeric members of the immunoglobulin superfamily found exclusively on the surface of cells capable of stimulating T cell growth. The receptor for B7 molecules on the T cell is CD28, yet another member of the immunoglobulin superfamily. Ligation of CD28 by B7-1 or B7-2 or by anti-CD-28 antibodies will co-stimulate the growth of naive T-cells, while antibodies to B7 molecules, which inhibit their binding to CD28, inhibit T cell responses [Specification, p. 3, para. 3].

Also, relevant to the present invention are mesenchymal stem cells. These cells are said to be the formative pluripotential blast cells found, inter alia, in bone marrow, blood, dermis and periosteum. Specification, p. 5, para. 1. Said stem cells "are capable of differentiating into any of the specific types of mesenchymal or connective tissues (i.e., the tissues of the body that support the specialized elements; particularly adipose, osseous, cartilaginous, elastic, and fibrous connective tissues) depending on various influences from bioactive factors, such as cytokines." Id. The present invention is said to be directed to inducing an antigen-specific T cell response using adipocytes or mesenchymal stem cells as antigen-presenting cells. Id., last para. The preferred T cell response is said to be a cytotoxic T cell (CTL) response. Id.

Discussion

In reviewing the applied prior art we find that Robinson discloses the construction of autologous, heterologous or xenogenic PAPCs (professional APCs),[1] and primary

[1] Robinson discloses that several different cell types can function as professional APCs. Robinson, col. 5, lines 36-37; col. 9, lines 31-35. These cell types are said to

cells that are not PAPCs,[2] as well as cell lines obtained from a variety of sources[3] which have been genetically engineered to express HLA molecules, costimulation molecules and immunoregulatory molecules[4] and selected antigens[5] in a manner which renders said cells capable of activating or suppressing T cells. Robinson, col. 1, lines 20-26;

---

include any vertebrate cell that functions physiologically to present antigens to T cells and cause T cell activation. Id., col. 9, lines 32-34. Such cells include, but are not limited to, "macrophages, monocytes, dendritic cells, Langerhans cells and activated B cells." Id., lines 34-35.

[2] Non-professional APCs are said to include other cell types which possess antigen-processing and antigen-presenting capabilities such as

> activated T cells, fibroblasts, eosinophils, keratinocytes, astrocytes, microglial cells, thymic cortical epithelial cells, endothelial cells, Schwann cells, retinal pigment epithelial cells, myoblasts, vascular smooth muscle cells, chondrocytes, enterocytes, thyrocytes and kidney tubule cells. These may be primary cells recently explanted from a host and not extensively passaged in cell culture to form an established cell line, or established cell lines that are relatively homogenous and capable of proliferating for many generations or indefinitely. Robinson, col. 9, lines 36-49.

[3] Robinson discloses that cell lines for use in the invention can be (i) obtained from a variety of sources such as the ATCC Catalogue of Cell Lines and Hybridomas; or (ii) produced using standard methods. Robinson, col. 10, lines 17-22.

[4] Robinson discloses that "costimulation molecules and other immunoregulatory proteins will include at least a portion of the coding sequence sufficient to provide the engineered cell with the desired function. For example, in the case of a costimulation molecule, a portion of the coding sequence that enables it to bind its ligand on T cells can be used." See, col. 17, lines 52-58 and claim 5.

[5] Robinson discloses that antigens of the invention include antigens or epitopes of infectious agents, cancer, transplantation antigens, allergens and autoantigens. See, col. 10, lines 25- col. 11, line 38.

col. 6, lines 5-8. Thus, said cells are capable of enhancing or suppressing immune responses to the antigens which they present. Id., col. 1, lines 25-26.

Thus, Robinson discloses cells which express at least one co-stimulatory molecule and at least one exogenous antigen fragment bound to a member of an MHCII molecule in a manner which induces an immune response in a host.

Gerson discloses that human mesenchymal cells can be genetically engineered to express exogenous gene products, particularly for the expression of physiologically or pharmacologically active proteins, or for use in gene therapy. Gerson, col. 1, lines 4-12. Gerson further discloses the advantages of employing genetically-engineered stem cells which include, inter alia, "the ability of newly introduced genes within human stem cells and their progeny to be expressed in a less restrictive fashion than other cells, thereby expanding the potential application in treating medical disease." Id., col. 3, lines 21-24.

The examiner argues that given the aforementioned advantage of using genetically-engineered human mesenchymal stem cells taught by Gerson, it would have been obvious to one of ordinary skill in the art to employ said stem cells as the primary non-professional antigen presenting cell in the manner taught by Robinson. Answer, p. 7. That is, it would have been obvious to transfect mesenchymal stem cells with a vector encoding B7-1 or B7-2, and to further modify said cells to present an antigen bound to an MHC class II molecule. Id.

It is well established that the examiner has the initial burden under 35 U.S.C. § 103 to establish a prima facie case. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Piasecki, 745 F.2d 1468, 1471-72, 223 USPQ 785, 787-88 (Fed. Cir. 1984). To that end, it is the examiner's responsibility to show that some objective teaching or suggestion in the applied prior art, or knowledge generally available in the art, would have led one of ordinary skill in the art to combine the references to arrive at the claimed invention. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 7 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

Here, we agree with the appellant[6] that although Robinson discloses many cell types which may be genetically engineered to render the cells capable of processing and presenting antigens to cells of the immune system of a subject, Robinson does not disclose or suggest the use of a mesenchymal stem cell, or cell of the adipocyte lineage, as set forth in representative claims 19 and 29. Although Gerson discloses that genetically-engineered mesenchymal stem cells can express various therapeutic agents, we find that the patent only discloses therapeutic agents which are used to treat diseases or disorders. That is, Gerson discloses the use of genetically-engineered stem cells to serve as "continuous drug delivery systems to replace present regimens, which require periodic administration (by ingestion, injection, depot infusion etc) of the needed substance." Gerson, col. 7, lines 55-59. Thus, we find the genes expressed in

[6] Brief, p. 4, first complete para.

the stem cells taught by Gerson and their application (gene therapy and production of pharmacologically-active compounds (see col. 10, lines 9-29)) to be radically different from the antigens said to be expressed by the claimed and their application (to induce an immune response). We do not find that the statement relied upon by examiner provides any suggestion to combine these teachings. Rather, the only mention we find of a mesenchymal stem cell, or a cell of the adipose lineage, which (i) expresses at least one co-stimulatory molecule, such as B7-1 or B7-2; and (ii) has been modified to have at least one exogenous antigen bound to an MHC class II moiety in a manner which initiates an immune response, is in the appellant's specification. Thus, we find that the examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention would have been obvious over Robinson and Gerson. In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1138, 227 USPQ 543, 547 (Fed. Cir. 1985); W.L. Gore & Assocs. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-313 (Fed. Cir. 1983)("To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher"). Accordingly, we reverse.

The decision of the examiner is reversed.

REVERSED

Joan Ellis Administrative Patent Judge	)
Toni R. Scheiner Administrative Patent Judge	) BOARD OF PATENT) APPEALS AND
Lora M. Green Administrative Patent Judge	) INTERFERENCES

JE/eld

Raymond J. Lillie, Esq
Carella, Byrne, Bain, Gilfillan, Cecchi,
Stewart & Olson
6 Becker Farm Rd.
Roseland, NJ 07068